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Application Number

08/234,145

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US006657103B1

(12) **United States Patent**  
Kucherlapati et al.(10) Patent No.: **US 6,657,103 B1**  
(45) Date of Patent: **\*Dec. 2, 2003**(54) **HUMAN ANTIBODIES DERIVED FROM  
IMMUNIZED XENOMICE**(75) Inventors: Raju Kucherlapati, Darien, CT (US);  
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(\*) Notice: This patent issued on a continued prosecution application filed under 37 CFR 1.53(d), and is subject to the twenty year patent term provisions of 35 U.S.C. 154(a)(2).

Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) Appl. No.: 08/923,138

(22) Filed: Sep. 4, 1997

**Related U.S. Application Data**

(63) Continuation of application No. 08/430,938, filed on Apr. 27, 1995, now abandoned, which is a continuation-in-part of application No. 08/234,145, filed on Apr. 28, 1994, now abandoned, which is a continuation-in-part of application No. 08/112,848, filed on Aug. 27, 1993, now abandoned, which is a continuation of application No. 08/031,801, filed on Mar. 15, 1993, which is a continuation-in-part of application No. 07/919,297, filed on Jul. 24, 1992, now abandoned, which is a continuation-in-part of application No. 07/610,515, filed on Nov. 8, 1990, now abandoned, which is a continuation-in-part of application No. 07/466,008, filed on Jan. 12, 1990, now abandoned.

(51) Int. Cl.<sup>7</sup> ..... C12P 21/00; A01K 67/027;  
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435/320.1

(58) Field of Search ..... 800/4, 6, 18; 435/320.1

(56) **References Cited****U.S. PATENT DOCUMENTS**4,816,397 A 3/1989 Boss et al. .... 435/68  
4,950,599 A 8/1990 Bertling ..... 435/172.3  
4,959,313 A 9/1990 Taketo ..... 435/69.1  
5,204,244 A 4/1993 Fell et al. .... 435/69.6  
5,545,806 A \* 8/1996 Lonberg et al. .... 800/2  
5,545,807 A \* 8/1996 Surani et al. .... 800/2  
5,569,824 A 10/1996 Donohower et al. .... 800/2  
5,569,825 A 10/1996 Lonberg et al. .... 800/2  
5,591,669 A \* 1/1997 Krimpenfort ..... 800/2  
6,150,584 A \* 11/2000 Kucherlapati et al. .... 800/18**FOREIGN PATENT DOCUMENTS**AU B-15172/95 7/1995  
EP 0 298 807 A1 6/1988  
EP 0 315 062 5/1989  
EP 0 322 240 6/1989  
EP 322240 6/1989  
EP 0 459 372 A3 5/1991EP 0 463 151 1/1992  
WO 90/04036 4/1990  
WO 91/00906 1/1991  
WO 91/10741 7/1991  
WO 92/03918 3/1992  
WO 93/05165 3/1993  
WO 94/00569 1/1994  
WO 94/02602 2/1994  
WO 96/33735 10/1996**OTHER PUBLICATIONS**Bruggeman et al. *PNAS* 82: 6709, 1989.\*  
Cox, declaration in 5, 545, 806.\*  
Dorfman, Nickolas A., 1985, "The Optimal Technological Approach to the Development of Human Hybridomas," *Journal of Biological Response Modifiers* 4:213-239.  
Taggart et al., 1983, "Stable Antibody-Producing Murine Hybridomas," *Science* 219:1228-1230.  
Albertsen, et al., Construction and characterization of a yeast artificial chromosome library containing seven haploid human genome equivalents, *Proc. Natl. Acad. Sci.* 87:4256-4260 (1990).  
Aldhous, "Transgenic mice display a class (switching) act," *Science* 262:1212-1213 (1993).  
Ayares, et al., "Sequence homology requirements for inter-molecular recombination in mammalian cells," *Proc. Natl. Acad. Sci.*, 83:5199-5203 (1986).  
Berman, et al., "Content and organization of the human Ig V<sub>H</sub> locus: definition of three new V<sub>H</sub> families and linkage to the Ig C<sub>H</sub> locus," *EMBO J.*, 7:727-738 (1988).  
Bird, et al., "Single-Chain Antigen-Binding Proteins," *Science*, 423-426 (1988).  
Blankenstein, et al., "Immunoglobulin V<sub>H</sub> region genes of the mouse are organized in overlapping clusters," *Eur. J. Immunol.*, 17:1351-1357 (1987).  
Brinster, et al., "Introns increase transcriptional efficiency in transgenic mice," *Proc. Natl. Acad. Sci.*, 85:836-840 (1988).  
Brownstein, et al., "Isolation of single-copy human genes from a library of yeast artificial chromosome clones," *Science*, 244:1348-1351 (1989).  
Bruggeman, et al., "Human antibody production in transgenic mice: expression from 100kb of the human IgH locus," *European Journal of Immunology*, 21:1323-1326 (1991).  
Bruggemann, et al., "Construction, function and immunogenicity of recombinant monoclonal antibodies," *Behring Inst. Mitt.*, 87:21-24 (1990).

(List continued on next page.)

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(57) **ABSTRACT**

Antibodies with fully human variable regions against a specific antigen can be prepared by administering the antigen to a transgenic animal which has been modified to produce such antibodies in response to antigenic challenge, but whose endogenous loci have been disabled. Various subsequent manipulations can be performed to obtain either antibodies per se or analogs thereof.

4 Claims, 18 Drawing Sheets